UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER OF PATENTS AND TRADEMARKS
Washington, D.C. 20231

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR		ATTORNEY DOCKET NO.
09/099,898	06/18/98	FRANZ-BACON	K	DX0744K

028008
DNAX RESEARCH INSTITUTE
LEGAL DEPARTMENT
901 CALIFORNIA AVENUE
PALO ALTO CA 94304

HM12/0411

EXAMINER	
WEGERT,S	
ART UNIT	PAPER NUMBER
1647	18

DATE MAILED: 04/11/01

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary	Application No. 09/099,898	Applicant(s) FRANZ-BACON ET AL.	
	Examiner Sandra Wegert	Art Unit 1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *22 January 2001* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *19-30* is/are pending in the application.

4a) Of the above claim(s) *29* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *19-28, 30* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

15) ☒ Notice of References Cited (PTO-892)
16) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
17) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
18) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
19) ☐ Notice of Informal Patent Application (PTO-152)
20) ☐ Other: .

DETAILED ACTION

Status of Application, Amendments, and/or Claims

The art unit and examiner in charge of this application have changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Examiner Sandra Wegert in Group Art Unit 1647.

The amendment filed Jan 22, 2001 (Paper No. 12) has been entered. Claims 1-18 were cancelled. Claims 19-30 were added and read on previously elected Invention VI (Claims 11-17).

Newly submitted claim 29 is directed to an invention that is independent or distinct from the invention originally claimed for the following reasons: it does not read upon the polynucleotide and expression system elected by the Applicant in Paper 8 . Claim 29 is related to the claimed Invention as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product (MPEP § 806.05(h)). In the instant case the polynucleotide can be used to make the polypeptide of SEQ ID NO:2.

Since applicant has received an action on the merits for the originally presented invention, this invention has been constructively elected by original presentation for prosecution on the merits. Accordingly, claim 29 is withdrawn from consideration as being directed to a non-elected invention. See 37 CFR 1.142(b) and MPEP § 821.03.

Claims 19-28 and 30 are currently under examination.

Withdrawn Objections and/or Rejections

The requirement for a new title set forth at p. 2 of the previous office action (Paper No. 11, 28 July 2000) is withdrawn in view of Applicant's amendment providing a new title (Paper No. 12, 22 Jan. 2001). The rejection of Claims 11-17 under 35 USC 112, 2nd ¶, set forth at pp. 2-5 of the previous office action (Paper No. 10) is withdrawn in view of the cancelled claims (Paper 12). The rejection of Claims 11-17 under 35 USC 112, 1st ¶, set forth at pp. 5-10 (Paper No. 10) is withdrawn in view of the cancelled claims (Paper 12). Likewise, the rejection of Claims 11, 16 and 17 under 35 USC §102(a) or (b), or alternatively, 103(a), set forth at pp. 10-11 (Paper No. 10) is withdrawn in view of the cancelled claims (Paper 12).

Claim Rejections - 35 USC § 101 and 35 USC § 112, first paragraph

The following is a quotation of 35 U.S.C. 101:

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 19-28 and 30 are rejected under 35 U.S.C. 101 because the claimed invention lacks a credible, specific and substantial asserted utility or a well-established utility.

The claims are directed to a nucleotide which encodes *C23*, a linear peptide of 103 amino acids that the Applicant asserts contains motifs linking it to a defensin, growth factor, cytokine, or chemokine (p. 8, line 28, for example). However, the specification does not disclose a function for the nucleotide encoding *C23* in the context of the cell or organism.

The applicant places the claimed sequence in the "CRSP" or "Cysteine Rich Soluble Protein" family, thus presumably conferring some structural and functional characteristics of a family of proteins. However, no such family of molecules exists. In addition, there is no consistent structural motif linking the claimed molecule with nucleotides encoding defensins, growth factors, chemokines, or cytokines.

No well-established utility exists for newly isolated complex biological molecules. However, the specification asserts the following as credible, specific and substantial patentable utilities for the claimed putative polynucleotide:

1) to probe standard restriction fragment polymorphism blots to aid in distinguishing between individuals;

2) for use in *in situ* assays to detect chromosomal abnormalities.

Each of these shall be addressed in turn.

1) to probe standard restriction fragment polymorphism blots to aid in distinguishing between individuals. This asserted utility may be credible, however it is neither specific nor substantial. Restriction fragment length polymorphisms (RFLP's) do sometimes distinguish between individuals, thus making this a somewhat credible assertion. However RFLP's are numerous and are randomly distributed throughout the genome, and often *do not* distinguish between individuals. RFLP's are better used for following genes through generations of families or through populations (i.e., Linkage Analyses of genetic diseases). An RFLP associated with

the Applicant's claimed sequence may exist in an unpredictable number of individuals, or in none. Applicants have not demonstrated the presence of *any* RFLP within or near the sequence claimed. Thus, the asserted utility is not substantial. Finally, many unrelated sequences can be used in RFLP's generally. Thus, the asserted utility is not specific.

2) for use in in situ assays to detect chromosomal abnormalities. This asserted utility may be credible depending on what is meant by "chromosomal abnormalities" but is neither substantial nor specific. Applicant may be referring to the use of a hybridization probe to detect chromosomal abnormalities within the gene of interest. However, probes and primers can be designed from any polynucleotide sequence, and thus the asserted utility is not specific. Further, the specification does not disclose specific cDNA, DNA, or RNA targets. Since this asserted utility is not present in mature form, so that it could be readily used in a real world sense, the asserted utility is not substantial.

Claim 27 is also rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter. Claim 27 reads on a product of nature in that the claimed polynucleotide is not "isolated".

Claims 19-28 and 30 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

Claims 19-28 and 30 are directed to an isolated nucleic acid molecule that encodes a polypeptide comprising the amino acid sequence of SEQ ID NO: 2. The claims also recite a nucleic acid molecule that has a nucleotide sequence comprising the nucleotides of SEQ ID

NO: 1. Further, the claims recite an expression vector comprising the nucleic acid molecule that produces the polypeptide having the amino acid sequence of SEQ ID NO:2, a recombinant host cell, a nucleotide that hybridizes to the polynucleotide of SEQ ID NO:1, and a process of producing a recombinant host cell and polypeptide.

The specification teaches the polynucleotide encoding *C23*. However, the specification does not teach functional or structural characteristics of the polynucleotide or *C23* recited in the claims.

Generally, the art acknowledges that function cannot be predicted based solely on structural similarity to a protein found in the sequence databases. For example, Skolnick et al. (2000, Trends in Biotech. 18:34-39) state that knowing the protein structure by itself is insufficient to annotate a number of functional classes, and is also insufficient for annotating the specific details of protein function (see Box 2, p. 36). Similarly, Bork (2000, Genome Research 10:398-400) states that the error rate of functional annotations in the sequence database is considerable, making it even more difficult to infer correct function from a structural comparison of a new sequence with a sequence database (see especially p. 399). Such concerns are also echoed by Doerks et al. (1998, Trends in Genetics 14:248-250) who state that (1) functional information is only partially annotated in the database, ignoring multi functionality, resulting in underpredictions of functionality of a new protein and (2) overpredictions of functionality occur because structural similarity often does not necessarily coincide with functional similarity. Smith et al. (1997, Nature Biotechnology 15:1222-1223) remark that there are numerous cases in which proteins having very different functions share structural similarity due to evolution from a common ancestral gene. Brenner (1999, Trends in Genetics 15:132-133) argues that accurate inference of function from homology must be a difficult problem since, assuming there are only about 1000 major gene superfamilies in nature, then most homologues must have different

molecular and cellular functions. Finally, Bork et al. (1996, Trends in Genetics 12:425-427) add that the software robots that assign functions to new proteins often assign a function to a whole new protein based on structural similarity of a small domain of the new protein to a small domain of a known protein. Such questionable interpretations are written into the sequence database and are then considered facts.

Therefore, based on the discussions above concerning the specific examples of structurally similar proteins that have different functions, along with the art's recognition that one cannot rely upon structural similarity alone to determine functionality, the specification fails to teach the skilled artisan how to use the claimed polynucleotides to make biologically active *C23* without resorting to undue experimentation to determine what the specific biological activities of the polypeptide are.

The specification does not teach the skilled artisan how to use the claimed polynucleotides encoding *C23* for *any* purpose. For example, there is no disclosure of particular disease states correlating to an alteration in levels or forms of the polypeptide such that the claimed polynucleotides encoding *C23* could be used as a diagnostic tool. Therefore, the skilled artisan is not provided with sufficient guidance to use the claimed polynucleotides for any purpose.

Due to the large quantity of experimentation necessary to determine an activity or property of the disclosed polypeptide such that it can be determined how to use the claimed polynucleotides encoding *C23* and to screen for activity, the lack of direction/guidance presented in the specification regarding same, the absence of working examples directed to same, the complex nature of the invention, the state of the prior art establishing that biological activity cannot be predicted based on structural similarity and the unpredictability of the effects of mutation on protein structure and function, and the breadth of the claims which fail to recite

particular biological activities, undue experimentation would be required of the skilled artisan to make and/or use the claimed invention in its full scope.

Furthermore, regarding Claim 19, the specification does not reasonably provide enablement for the polynucleotide encoding the *mature* polypeptide of SEQ ID NO:2. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims. Applicants have not described any details of the polynucleotide or polypeptide, such as leader sequences or processing sites; therefore, details about the *mature* polypeptide of SEQ ID NO:2 are not known.

Claims 19-28 and 30 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention.

Claims 19-28 and 30 are directed to an isolated nucleic acid molecule that encodes a polypeptide comprising the amino acid sequence of SEQ ID NO: 2. The claims also recite a nucleic acid molecule that has a nucleotide sequence comprising the nucleotides of SEQ ID NO: 1. Further, the claims recite an expression vector comprising the nucleic acid molecule that produces the polypeptide having the amino acid sequence of SEQ ID NO:2, a recombinant host cell, a nucleotide that hybridizes to the polynucleotide of SEQ ID NO:1, and a process of producing a recombinant host cell and polypeptide.

The specification teaches a human *C23* polynucleotide and polypeptide (SEQ ID NO: 1 and SEQ ID NO: 2, respectively). However, the specification does not teach functional or

structural characteristics of isolated polynucleotides. The description of one *C23* polynucleotide species (SEQ ID NO: 1) and one *C23* polypeptide species (SEQ ID NO: 2) is not adequate written description of an entire genus of functionally equivalent polynucleotides and polypeptides.

Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, clearly states that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed"* (See page 1117). The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed" (See *Vas-Cath* at page 1116).

With the exception of the sequences referred to above, the skilled artisan cannot envision the detailed chemical structure of the encompassed polynucleotides, and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of isolating it. The nucleic acid itself is required. See *Fiers v. Revel*, 25 USPQ2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016.

One cannot describe what one has not conceived. See *Fiddes v. Baird*, 30 USPQ2d 1481 at 1483. In *Fiddes*, claims directed to mammalian FGF's were found to be unpatentable due to lack of written description for that broad class. The specification provided only the bovine sequence.

Therefore, only an isolated nucleic acid molecule comprising the nucleotide sequence of SEQ ID NO: 1 and a polypeptide comprising the amino acid sequence of SEQ ID NO:2, but not the full breadth of the claims, meets the written description provision of 35 U.S.C. §112, first

paragraph. Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 U.S.C. §112 is severable from its enablement provision (see page 1115).

35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

Claim 27 is rejected under 35 U.S.C. 102(a) as being anticipated by Adams, M. et al (1997, Acc. No. AA311223). Claim 27 recites a polynucleotide that hybridizes to the polynucleotide of Claim 19, under hybridization conditions of 55° C and 150mM salt, and wash conditions of 30° C and less than 2M salt. Adams, M., et al, teach a mRNA that is more than 93% homologous to a polynucleotide which hybridizes to the polynucleotide of Claim 19. Since Claim 27 claims sequences that hybridize to the polynucleotide of Claim 19, under the hybridization conditions specified, the polynucleotide cited by Adams, et al falls within the limits of the claim.

Conclusion

Claims 19-28, and 30 are rejected.

It was noted at the end of the Applicants' Amendment and Response (Paper 12) that an interview was requested. Due to the length of the instant office action, it could only be submitted in writing, therefore applicant is invited to request an oral interview upon receipt of this Paper.

Advisory Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sandra Wegert whose telephone number is (703) 308-9346. The examiner can normally be reached Monday - Friday from 8:30 AM to 5:00 PM (Eastern Time).

If attempts to reach the examiner by telephone are unsuccessful, the Examiner's supervisor, Gary Kunz, can be reached at (703) 308-4623.

Official papers filed by fax should be directed to (703) 308-4242. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Elizabeth C. Kemmerer

SLW

4/8/01

ELIZABETH KEMMERER
PRIMARY EXAMINER